INSTRUMENT FOR MONITORING POLYMERASE CHAIN REACTION OF DNA

This application claims the benefit of provisional applications No. 60/085,765, filed 5-16-98, and 60/092,784, filed 7-14-98.

This invention relates to biochemical analyses, and particularly to quantitative monitoring of DNA during a polymerase chain reaction (PCR) process.

BACKGROUND

Polymerase chain reaction (PCR) is a process for amplifying or multiplying quantities of double-stranded deoxyribonucleic acid (DNA). In a PCR apparatus, a thermal cycler block has one or more wells for holding vials containing a suspension of ingredients for a reaction to produce more DNA starting with "seed" samples of the DNA. The starting ingredients in an aqueous suspension, in addition to the a seed sample, include selected DNA primer strands, DNA elements, enzymes and other chemicals. The temperature of the block is cycled between a lower temperature extension phase of the PCR reaction at about 60°C, which is the phase where all of the DNA strands have recombined into double strands, and a high temperature denaturing phase at about 95°C, during which the DNA is denatured or split into single strands. Such a temperature program essentially doubles the DNA in each cycle, thus providing a method for replicating significant amounts of the DNA from a small starting quantity. The PCR process is taught, for example, in U.S. patent No. 4,683,202.

Quantitative measurements have been made on the DNA production during the PCR process, to provide measures of the starting amount and the amount produced. Measurements and computation techniques are taught in U.S. patent No. 5,766,889 (Atwood), as well as in an article "Kinetic PCR Analysis: Real-time Monitoring of DNA Amplification Reactions" by Russel Higuchi, et al., Bio/Technology vol. 11, pp. 1026-1030 (September 1993), and an article "Product Differentiation by Analysis of DNA Melting Curves during the Polymerase Chain Reaction" by Kirk M. Ririe, et al., Analytical Biochemistry vol. 245, pp. 154-160 (1997).